CLAIMS

1. Use of a compound of Formula (I), a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a compound of Formula (I) in the preparation of a medicament for the prevention of symptomatic *P. falciparum* malaria in a human subject after potential exposure of the subject to mosquitoes carrying *P. falciparum* malaria, wherein the medicament is formulated for administration according to a dosage regime, said dosage regime comprising:

a) administering to the human subject two or more primary doses of a compound of Formula (I), a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a compound of Formula (I), wherein the primary doses are administered prior to or during potential exposure to *P. falciparum* and wherein at least the first primary dose is administered prior to potential exposure of the subject to *P. falciparum*; and

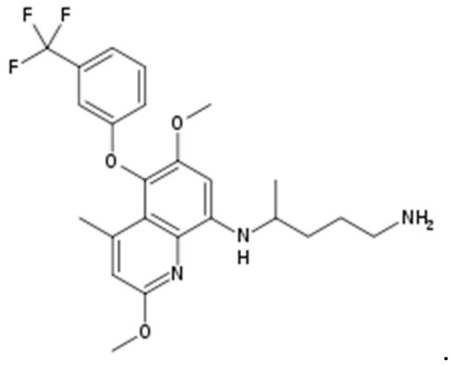
b) administering to the human subject one or more post-exposure dose(s) of a compound of Formula (I), a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a compound of Formula (I), wherein said post-exposure dose is administered within ~~1-10 days~~one week after the risk of potential exposure to *P. falciparum*,

wherein each primary dose is about 75 to about 399 mg and wherein each post-exposure dose is about 75 to about 399 mg,

wherein said primary dose comprises one or more individual doses sufficient to achieve a serum or plasma concentration of at least about 80 ng/mL of a compound of Formula (I), and wherein said post-exposure dose comprises one or more individual doses sufficient to maintain for at least three weeks after potential exposure of the subject to *P. falciparum*, a serum or plasma concentration of at least about 80 ng/mL of a compound of Formula (I),

wherein the human subject is malaria-naïve and Glucose-6-phosphate dehydrogenase (G6PD) normal, and

wherein Formula (I) has the following structure,



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2. The use of claim 1, wherein a serum or plasma concentration of at least about 80 ng/mL of a compound of Formula (I) is attained prior to potential exposure, maintained during potential exposure, and maintained for at least three weeks after potential exposure of the subject to *P. falciparum*.

3. The use of claim 2, wherein the serum or plasma concentration of at least about 80 ng/mL of a compound of Formula (I) is measured in the individual human subject.

4. The use of any one of claims 2 or 3, wherein the Cmin serum or plasma concentration of at least about 80 ng/mL of a compound of Formula (I) is measured as the median Cmin of a population of subjects administered the given dose of a compound of Formula (I).

5. The use of any one of claims 1 to 4, wherein the primary dose is administered three times.

6. Use of a compound of Formula (I), a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a compound of Formula (I) in the preparation of a medicament for the prevention of symptomatic *P. falciparum* malaria in a human subject, wherein the medicament is formulated for administration according to a dosage regime, said dosage regime comprising:

a) administering to the human subject two or more initial doses of a compound of Formula (I), a pharmaceutically acceptable salt thereof, or a pharmaceutical

composition comprising a compound of Formula (I), wherein at least the first initial dose is administered prior to potential exposure of the subject to *P. falciparum*;

b) administering to the human subject an exposure dose of a compound of Formula (I), a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a compound of Formula (I), one or more times per week during potential exposure of the subject to *P. falciparum*; and

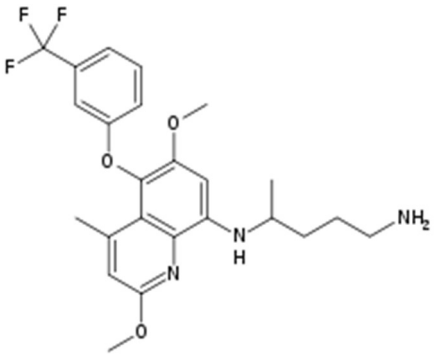
c) administering to the human subject one or more post-exposure dose(s) of a compound of Formula (I), a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising a compound of Formula (I), within ~~1-10 days~~one week after the risk of potential exposure to *P. falciparum* has substantially ended ,

wherein each said initial dose is about 75 to about 299 mg, wherein the total combined amount of said compound of Formula (I) administered in said initial doses is about 500 mg to about 900 mg, wherein the total administered amount of the exposure dose is about 75 to about 299 mg per week, and wherein each said post-exposure dose is about 40 to about 399 mg,

wherein a serum or plasma concentration of at least about 80 ng/mL of Formula (I) is attained prior to potential exposure, maintained during potential exposure, and maintained for at least three weeks after potential exposure of the subject to *P. falciparum*,

wherein the human subject is malaria-naïve and Glucose-6-phosphate dehydrogenase (G6PD) normal, and

wherein Formula (I) has the following structure,



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7. The use of any one of claims 1-6, wherein the post-exposure dose comprises three individual doses.

8. The use of claim 7, wherein the individual post-exposure doses are given on three consecutive days or given once per week for three consecutive weeks.

9. The use of any one of claims 6-8, wherein the initial dose is about 150 mg, the total administered amount of the exposure dose is about 150 mg per week, and the post-exposure dose is about 150 mg.

10. The use of any one of claims 6-8, wherein each initial dose is about 200 mg, the total administered amount of the exposure dose is about 200 mg per week, and each post-exposure dose is about 200 mg.

11. The use of any one of claims 6-8, wherein the initial dose is between about 75 and about 175 mg, the total administered amount of exposure dose is between about 75 and about 175 mg per week, and the post-exposure dose is between about 75 and about 175 mg.

12. The use of any one of claims 6-11, wherein the initial dose is administered once per day for three days prior to potential exposure, and the post-exposure dose is administered once per week for three weeks after potential exposure.

13. The use of any one of claims 6-11, wherein the initial dose is administered once per day for three days prior to potential exposure, and the post-exposure dose is administered once per day for three days.

14. The use of any one of claims 6-11, wherein the initial dose is administered three times and the post-exposure dose is administered once per week for three weeks.

15. The use of any one of claims 6-11, wherein the initial dose is administered three times and the post-exposure dose is administered once per day for three days.

16. The use of any one of claims 6-15, wherein the exposure dose is a daily dose of 25 mg.

17. The use of any one of claims 1-16, wherein the subject has low body weight or age and the compound of Formula (I) is administered in a suitable formulation of about 75 to about 299 mg or about 1-5 mg/kg.

18. The use of any one of claims 6-17, wherein the total amount of the initial dose administered does not exceed about 600 mg prior to potential exposure of *P. falciparum*, and the total administered amount of the exposure dose does not exceed about 200 mg per week.

19. The use of claim 18, wherein the initial dose is about 40 to about 100 mg administered once per day for six days, and the exposure dose is about 10 mg, about 12 mg, about 15 mg, about 20 mg, about 25mg, or about 30 mg administered once per day.

20. The use of claim 18 or claim 19, wherein the initial dose is about 100 mg administered once per day for six days, and the exposure dose is about 100 mg administered every four days.

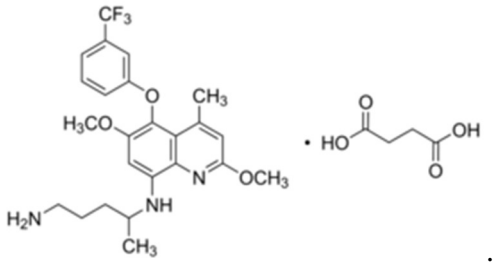
21. The use of any one of claims 6-17, wherein the total pre-exposure dose is about 240 to about 600 mg, and the exposure dose does not exceed 299 mg per week, and wherein the exposure dose is about 10 mg, about 12, mg, about 15 mg, about 20mg, about 30 mg, about 35 mg, about 40 mg, or about 42 mg administered once per day.

22. The use of any one of claims 1-21, wherein the compound, or the pharmaceutical composition, is administered orally or sublingually.

23. The use of any one of claims 1-21, wherein the human subject is a child.

24. The use of any one of claims 1-23, wherein the compound of Formula (I) is tafenoquine.

25. The use of any one of claims 1-24, wherein the pharmaceutical salt thereof is a salt of tafenoquine or a salt having the following structure,


CF3
O
CH3
H3CO
N
OCH3
NH
H2N
CH3
HO
O
OH
O

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